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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/463,075	01/14/2000	DANIEL COHEN	GENSET.020AP	5833

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EXAMINER

SISSON, BRADLEY L

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 08/16/2002

24

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/463,075

Applicant(s)

COHEN ET AL.

Examiner

Bradley L. Sisson

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 June 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 86,88,89 and 92-122 is/are pending in the application.
- 4a) Of the above claim(s) 106-122 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 86,88,89 and 92-105 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- ☐ Interview Summary (PTO-413) Paper No(s) _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Location of Application

1. The location of the subject application has changed. The subject application is now located in Group 1630, Art Unit 1634.

Election/Restrictions

2. Acknowledgement is made of applicant having added, through their response of 03 June 2002, new claim 122, which is drawn to a map. The invention of claim 122 would be properly combined in Group III, drawn to a map (See page 2 of Paper No. 8, mailed 14 September 2000). As demonstrated in the Office action of 14 September 2000, the claims of the subject application lack unity of invention and as such, may be properly restricted. Accordingly, claim 122 has been withdrawn from consideration, as it is not drawn to elected invention of Group I, a method of obtaining a plurality of single nucleotide polymorphisms.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 86, 88, 89, and 92-105 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goelet et al. (WO 95/12607), in view of Wang et al.

7. Goelet et al., disclose a method whereby single nucleotide polymorphisms (SNPs) can be detected in any plant or animal, including humans, and that these sites are useful in determining "identity, ancestry, predisposition to genetic disease, the presence or absence of a desired trait, etc." (Abstract). Goelet et al., page 14, first paragraph, teach that SNPs occur "approximately once every 300 bases in the mammalian genome, and exhibit uniformity of distribution, a SNP can, statistically, be found within 150 bases of any particular genetic lesion or mutation. Indeed, the particular mutation may itself be an SNP. Thus, where such locus has been sequenced, the

variation in that locus' nucleotide is determinative of the trait in question." Such a disclosure meets the limitation that the polymorphisms have a heterozygosity rate of "at least about 0.18 and having a mean inter-marker spacing of less than 50 kb" (claim 86).

8. As presently worded, claim 86 requires that the genomic library comprise either a) the entire human genome; or b) fragments that comprise at least 100 kb of continuous genomic DNA. Goelet is considered to meet this limitation where at page 13 they teach that their invention allows for the determination of a genetic map of SNPs in humans. The aspect of the genetic map being that of the entire genome is considered to be met by page 16 and Figure 1 where the entire genome of the individual is used to create a genomic library.

9. The aspect of ordering the fragments generate is met by the disclosure of Goelet et al., at page 18 where it is explicitly taught that the restriction profiles are generated and subsequently used in comparisons of other restriction ordered (restriction) patterns of DNA fragments. See also page 19 as yet another method for ordering fragments is disclosed.

10. The aspect of performing "high volume testing applications" is disclosed at page 31. Such a disclosure is considered to provide guidance and motivation for skilled artisan to scale up the method of identifying SNPs. Accordingly, the aspect of scaling up the disclosed method so that the entire genome of a human would be evaluated for SNPs would have been obvious to one of ordinary skill in the art.

11. The aspect of identifying those SNPs that have some value, e.g., "useful in determining identity, ancestry, predisposition to genetic disease, the presence or absence of a desired trait, etc." is disclosed at page 3.

12. With a single library of Goelet et al., giving rise to 5,000 SNPs ((500 individual clones x 3,000 b) / 300 b/SNP), and with a single library providing an analysis of but a small portion of the human genome, and with Goelet et al., fairly teaching that the entire genome can be scanned for SNPs, the aspect of one of skill in the art identifying "at least 20,000 single nucleotide polymorphisms" (claim 94) is fairly suggested.
13. The aspect of performing genetic analysis so as to determine if SNPs are in linkage equilibrium, or disequilibrium, is disclosed at pages 36-45.
14. Goelet et al., do not explicitly teach the heterozygosity rate of claims 92 and 93, however, the heterozygosity rate is that of the SNPs to be identified and are an inherent characteristic of the human DNA being evaluated. Since Goelet et al., fairly teach identifying all SNPs of any animal, including that of humans, the SNPs being identified would have as an inherent property, the heterozygosity rates set forth of claims 86, 92 and 93, and by extension, any claim that depends therefrom.
15. Wang et al., disclose producing "third generation map of the human genome consisting of bi-allelic single nucleotide polymorphisms (SNPs). They report that the SNPs have a minor allele frequency greater than 30% and appear to occur at the rate of 1/1000 bp. Such a showing is considered to meet the limitation of applicant's recite heterozygosity rate "of at least about 0.18" and "inter-marker spacing of less than 50 kb."
16. In view of the teachings of the prior art of record, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Goelet et al., with that of Wang et al., such that the entire human genome would be mapped and

that SNPs of value, and having the recited rate of heterozygosity and inter-marker distance would be identified.

Response to argument

17. At page 3 of the response received 03 June 2002 argument is advanced that "[I]n contrast, Goelet does not provide a method for selectively identifying SNPs with any desired property, but rather simply teaches the random selection of claimed from a genomic library and the subsequent sequencing of all or part of these clones in a plurality of individuals to identify SNPs."

18. The above argument has been fully considered and has not been found persuasive towards the withdrawal of the rejection. As set forth above, and found at page 32 of Goelet et al., a method is disclosed whereby SNPs of interest/value can be identified. While the order in which the fragments are taken for evaluation may be random, the evaluation of the entire genome, and especially in light of the ordering of the fragments, would unquestionably allow for the evaluation of the entire genome, and thereby meet applicant's requirement of evaluating a genomic DNA of at least 100 kb in length.

19. At page 4 of the response of 03 June 2002 argument is advanced that the rejection does not adequately teach how the method of Goelet et al., could be scaled up so to identify all of the SNPs in any animal, including that of a human. This argument has not been found persuasive for at page 3 of the response, applicant seeming is in agreement that Goelet et al., does teach sequencing all of the fragments of any one or more individuals and the identification of SNPs found in those fragments. Seemingly, therefore, Goelet et al., does adequately teach that the method disclosed can be scaled up so to allow for the identification of SNPs in the entire genome of an individual. Further to the point, and as indicated above, Goelet et al., teaches that the

method can be modified so to permit "high volume" screening. Additionally, the publication of Wang et al., clearly teaches that they have produced a third generation map of SNPs found in the human genome. Clearly, the aspect of performing an assay whereby the entire human genome could be evaluated for SNPs that have utility was known and had been performed.

20. For the above reasons, and in the absence of convincing evidence to the contrary, the invention of claims 86, 88, 89, and 92-105 is made obvious by the prior art of record.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

22. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

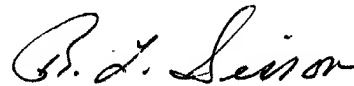
23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

Application/Control Number: 09/463,075
Art Unit: 1634

Page 8

24. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

25. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Bradley L. Sisson
Primary Examiner
Art Unit 1634

BLS
August 15, 2002